

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
 NEWS 2 Apr 08 "Ask CAS" for self-help around the clock
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 NEWS 7 Apr 22 BIOSIS Gene Names now available in TOXCENTER
 NEWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available
 NEWS 9 Jun 03 New e-mail delivery for search results now available
 NEWS 10 Jun 10 MEDLINE Reload
 NEWS 11 Jun 10 PCTFULL has been reloaded
 NEWS 12 Jul 02 FOREGE no longer contains STANDARDS file segment
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 saved answer sets no longer valid
 NEWS 14 Jul 29 Enhanced polymer searching in REGISTRY
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 NEWS 16 Aug 08 CANCERLIT reload
 NEWS 17 Aug 08 PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18 Aug 08 NTIS has been reloaded and enhanced
 NEWS 19 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)
 now available on STN
 NEWS 20 Aug 19 IFIPAT, IFICDB, and IFIUDB have been reloaded
 NEWS 21 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded
 NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced
 NEWS 23 Sep 03 JAPIO has been reloaded and enhanced
 NEWS 24 Sep 16 Experimental properties added to the REGISTRY file
 NEWS 25 Sep 16 Indexing added to some pre-1967 records in CA/CAPLUS
 NEWS 26 Sep 16 CA Section Thesaurus available in CAPLUS and CA
 NEWS 27 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985
 NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,
 CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
 AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
 NEWS HOURS STN Operating Hours Plus Help Desk Availability
 NEWS INTER General Internet Information
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 NEWS PHONE Direct Dial and Telecommunication Network Access to STN
 NEWS WWW CAS World Wide Web Site (general information)

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 20:08:06 ON 03 OCT 2002

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COST IN U.S. DOLLARS	SINCE FILE	TOTAL
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FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 20:08:18 ON 03 OCT 2002
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 2 OCT 2002 HIGHEST RN 458522-67-3
DICTIONARY FILE UPDATES: 2 OCT 2002 HIGHEST RN 458522-67-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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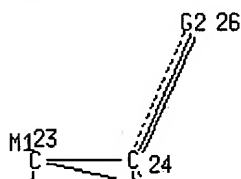
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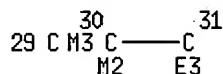
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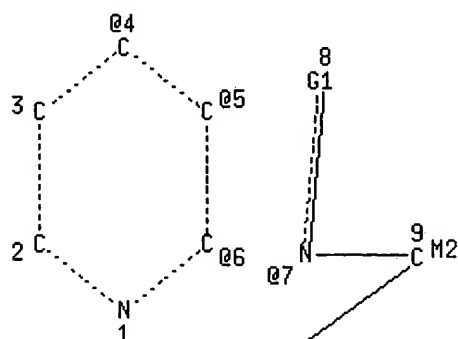


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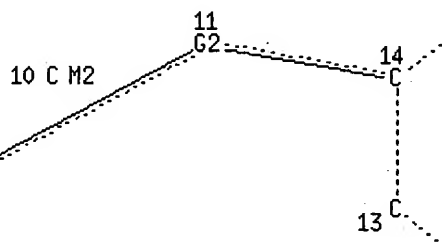
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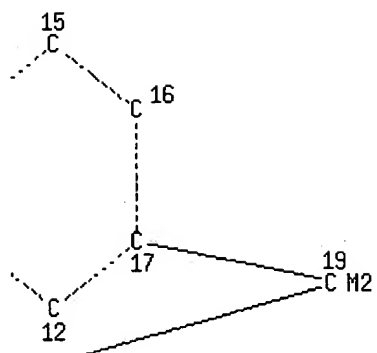


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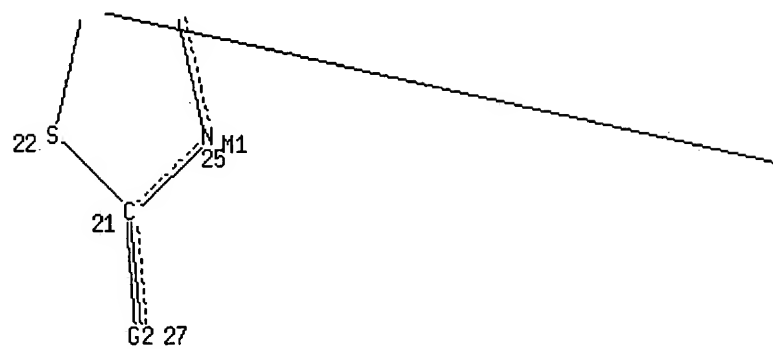


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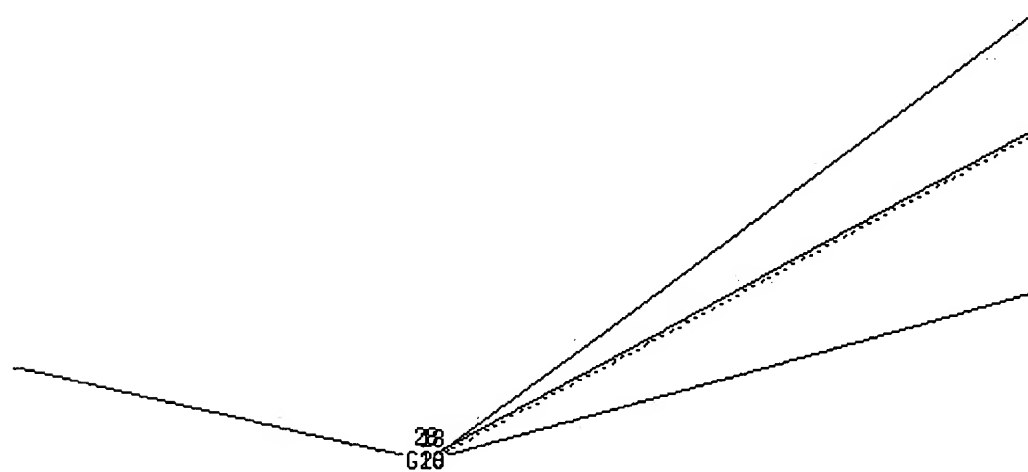


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VAR G2=32/33

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REP G20=(0-1) 10-9 10-11

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GRAPH ATTRIBUTES:

RSPEC I
NUMBER OF NODES IS 33

STEREO ATTRIBUTES: NONE

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100.0% PROCESSED 10 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.02

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 11 TO 389
PROJECTED ANSWERS: 2 TO 124

L2 2 SEA SSS SAM L1

=> s 11 full
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 139.90 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
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FULL SCREEN SEARCH COMPLETED - 310 TO ITERATE

100.0% PROCESSED 310 ITERATIONS 48 ANSWERS
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L3 48 SEA SSS FUL L1

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FILE 'HCAPLUS' ENTERED AT 20:14:30 ON 03 OCT 2002
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FILE COVERS 1907 - 3 Oct 2002 VOL 137 ISS 14
FILE LAST UPDATED: 2 Oct 2002 (20021002/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

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L4 490 L3

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L5      324 L3/THU
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L9      17 L8 AND PD < MAY 20 1999

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L9 ANSWER 1 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 2000:362595 HCAPLUS
DOCUMENT NUMBER: 133:13403
TITLE: Adipocyte containing ob gene promoter for screening modulators useful in treatment of anorexia, obesity, and other diseases
INVENTOR(S): Briggs, Michael R.; Auwerx, Johan; De Vos, Piet; Staels, Bart; Croston, Glenn E.; Miller, Stephen G.
PATENT ASSIGNEE(S): Ligand Pharmaceuticals Inc., USA
SOURCE: U.S., 64 pp., Cont.-in-part of U.S. Ser. No. 558,588, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6068976	A	20000530	US 1996-618100	19960319
<u>CA 2215387</u>	AA	19960926	<u>CA 1996-2215387</u>	<u>19960319</u>
PRIORITY APPLN. INFO.:				
			US 1995-408584	B2 19950320
			US 1995-418096	B2 19950405
			US 1995-510584	B2 19950802
			US 1995-558588	B2 19951030
			US 1995-7390P	P 19951121
			US 1995-7721P	P 19951130
			US 1995-8601P	P 19951214

AB This invention relates to the isolation and cloning of the promoter and other control regions of a human ob gene. It provides a **method** for identifying and screening for agents useful for the treatment of diseases and pathol. conditions affected by the level of expression of an ob gene. These agents interact directly or indirectly with the promoter or other

control regions of the ob gene. A PPAR γ agonist, BRL49653, has been identified to be useful in treating anorexia, cachexia, and other diseases characterized by insufficient food intake or body wt. loss. Modulators of ob gene expression may be used to treat other diseases such as obesity, **diabetes**, hypertension, cardiovascular diseases and infertility.

IT 122320-73-4, BRL49653

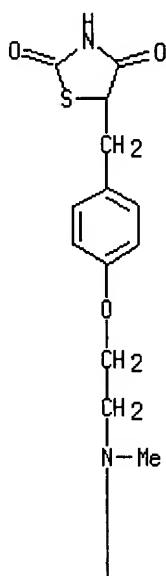
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(PPAR γ agonist; adipocyte contg. ob gene promoter for screening modulators useful in treatment of anorexia, obesity, and other diseases)

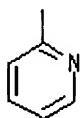
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



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REFERENCE COUNT:

9

THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 1999:316557 HCAPLUS

DOCUMENT NUMBER: 130:332912

TITLE: Activators of the nuclear orphan receptor peroxisome proliferator-activated receptor gamma for treatment of **diabetes** and cardiovascular disorders

INVENTOR(S): Kliewer, Steven Anthony; Lehmann, Jurgen M.; Willson, Timothy M.

PATENT ASSIGNEE(S): Glaxo Wellcome Inc., USA

SOURCE: U.S., 9 pp., Cont. of U.S. Ser. No. 804,310, abandoned.

CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>US 5902726</u>	A	19990511	<u>US 1998-28988</u>	19980225
<u>US 5994554</u>	A	19991130	<u>US 1998-207936</u>	19981209
PRIORITY APPLN. INFO.:			US 1994-363482	19941223
			US 1995-386394	19950210
			US 1997-804310	19970221
			US 1998-28988	19980225

OTHER SOURCE(S): MARPAT 130:332912

AB The present invention provides activator compds., including agonists, to the peroxisome proliferator-activated receptor gamma. Particular PPAR γ activators are set forth, as are a pharmaceutical compn. for treating **diabetes**, non-insulin-dependent **diabetes mellitus**, cardiovascular disorders, and **methods** for such treatment. Also claimed is a **method** of identifying activator compds.

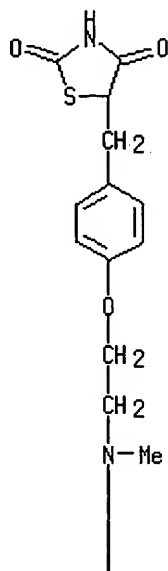
IT 173792-21-7

RL: ARG (Analytical reagent use); THU (Therapeutic use); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses) (for identifying PPAR γ -interacting compds. useful as drugs; activators of peroxisome proliferator-activated receptor gamma for treatment of **diabetes** and cardiovascular disorders)

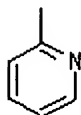
RN 173792-21-7 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, labeled with tritium (9CI) (CA INDEX NAME)

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REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 1999:167677 HCAPLUS
 DOCUMENT NUMBER: 131:124868
 TITLE: Systemic exposure to rosiglitazone is unaltered by food
 AUTHOR(S): Freed, M. I.; Allen, A.; Jorkasky, D. K.; DiCicco, R. A.
 CORPORATE SOURCE: SmithKline Beecham Clinical Pharmacology Unit, Presbyterian Medical Center of the University of Pennsylvania Health System, 51 North 39th Street, Philadelphia, PA, 19104, USA
 SOURCE: European Journal of Clinical Pharmacology (1999), 55(1), 53-56
 CODEN: EJCPAS; ISSN: 0031-6970
 PUBLISHER: Springer-Verlag
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Objective: To evaluate the effect of food on the bioavailability and pharmacokinetics of the insulin sensitizer rosiglitazone. **Methods:** In a randomized, open-label, period-balanced, single-dose, crossover study, rosiglitazone 2 mg was administered to 12 healthy male volunteers either in the fasting state or following a std. high-fat breakfast. The primary end points of the study were AUC_{0-inf} and C_{max}. Results: Single oral doses of rosiglitazone were safe and well tolerated. Overall exposure to rosiglitazone was unaffected by food. The geometric mean ratio of AUC_{0-inf} in the fed:fasted regimens was 0.94 (95% CI: 0.82, 1.06); t_{1/2} was unaffected. Absorption of rosiglitazone in the fed state was more gradual and sustained than in the fasted state. C_{max} was reduced by approx. 20% (point est. 0.80; 95% CI 0.65 to 0.97) and t_{max} was modestly delayed in the fed state. Conclusion: These data support dosing guidelines that will permit the administration of rosiglitazone without regard to meals for treatment of type 2 **diabetes mellitus**.

IT 122320-73-4, Rosiglitazone

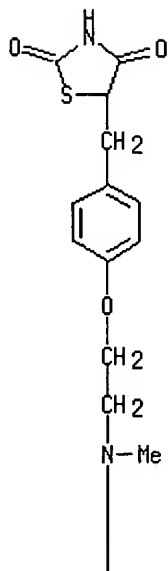
RL: BPR (Biological process); BSU (Biological study, unclassified);
 THU (**Therapeutic use**); BIOL (Biological study); PROC (Process);
 USES (Uses)

(bioavailability of antidiabetic rosiglitazone is unaltered by food intake in humans)

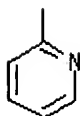
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 1999:81575 HCAPLUS
DOCUMENT NUMBER: 130:134189
TITLE: Treatment of **diabetes** with a thiazolidinedione, an insulin secretagogue, and an α -glucosidase inhibitor
INVENTOR(S): Buckingham, Robin Edwin; Smith, Stephen Alistair
PATENT ASSIGNEE(S): Smithkline Beecham PLC, UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 9903478</u>	<u>A1</u>	<u>19990128</u>	<u>WO 1998-GB2112</u>	<u>19980716</u>
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RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
<u>AU 9884490</u>	<u>A1</u>	<u>19990210</u>	<u>AU 1998-84490</u>	<u>19980716</u>
<u>EP 1001784</u>	<u>A1</u>	<u>20000524</u>	<u>EP 1998-935129</u>	<u>19980716</u>

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, FI, RO

BR 9810292	A	20000919	BR 1998-10292	19980716
JP 2001510160	T2	20010731	JP 2000-502777	19980716
ZA 9806364	A	20000117	ZA 1998-6364	19980717
NO 2000000230	A	20000117	NO 2000-230	20000117
US 2002052324	A1	20020502	US 2001-989572	20011120

PRIORITY APPLN. INFO.:

GB 1997-15298	A	19970718
WO 1998-GB2112	W	19980716
US 1999-445908	A1	19991215

AB A **method** and compn. are disclosed for the treatment of **diabetes mellitus** and conditions assocd. with **diabetes mellitus** in a mammal. The **method** comprises administering an effective nontoxic and pharmaceutically acceptable amt. of an insulin sensitizer, an insulin secretagogue and an α -glucosidase inhibitor antihyperglycemic agent to a mammal in need thereof.

IT **122320-73-4**

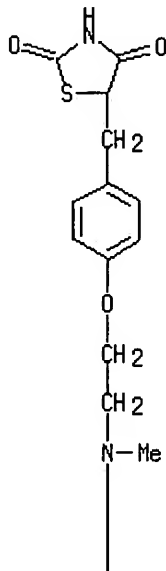
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(thiazolidinedione, insulin secretagogue, and α -glucosidase inhibitor for **diabetes** treatment)

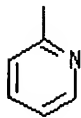
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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REFERENCE COUNT:

7

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 1999:81574 HCAPLUS
DOCUMENT NUMBER: 130:134188
TITLE: Treatment of **diabetes** with a thiazolidinedione, an insulin secretagogue, and a biguanide
INVENTOR(S): Buckingham, Robin Edwin; Smith, Stephen Alistair
PATENT ASSIGNEE(S): Smithkline Beecham PLC, UK
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 9903477</u>	<u>A1</u>	<u>19990128</u>	<u>WO 1998-GB2110</u>	<u>19980716</u>
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<u>AU 9884488</u>	<u>A1</u>	<u>19990210</u>	<u>AU 1998-84488</u>	<u>19980716</u>
<u>EP 1001783</u>	<u>A1</u>	<u>20000524</u>	<u>EP 1998-935127</u>	<u>19980716</u>
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
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			<u>WO 1998-GB2110</u>	<u>W 19980716</u>
			<u>US 1999-446039</u>	<u>A1 19991215</u>

AB A **method** and compn. are disclosed for the treatment of **diabetes mellitus** and conditions assocd. with **diabetes mellitus** in a mammal. The **method** comprises administering an effective nontoxic and pharmaceutically acceptable amt. of an insulin sensitizer, an insulin secretagogue and a biguanide antihyperglycemic agent to a mammal in need thereof.

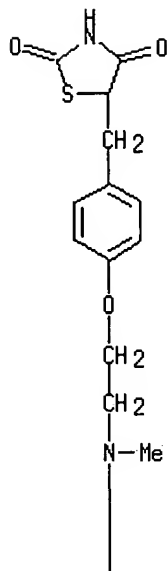
IT 122320-73-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(thiazolidinedione, insulin secretagogue, and biguanide for **diabetes** treatment)

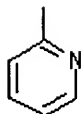
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 1999:81573 HCAPLUS
DOCUMENT NUMBER: 130:134187
TITLE: Treatment of **diabetes** with insulin sensitizer thiazolidinedione and insulin secretagogue sulfonylurea
INVENTOR(S): Buckingham, Robin Edwin; Smith, Stephen Alistair
PATENT ASSIGNEE(S): Smithkline Beecham PLC, UK
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 9903476</u>	<u>A1</u>	<u>19990128</u>	<u>WO 1998-GB2109</u>	<u>19980716</u>
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
<u>AU 9884487</u>	<u>A1</u>	<u>19990210</u>	<u>AU 1998-84487</u>	<u>19980716</u>
<u>AU 743269</u>	<u>B2</u>	<u>20020124</u>		

EP 998291	A1	20000510	EP 1998-935126	19980716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
BR 9810904	A	20000926	BR 1998-10904	19980716
JP 2001510158	T2	20010731	JP 2000-502775	19980716
ZA 9806365	A	20000117	ZA 1998-6365	19980717
NO 2000000229	A	20000117	NO 2000-229	20000117
US 2002045649	A1	20020418	US 2001-975883	20011012

PRIORITY APPLN. INFO.:

GB 1997-15306	A	19970718
WO 1998-GB2109	W	19980716
US 1999-445907	A1	19991215

AB A **method** for the treatment of **diabetes mellitus** and conditions assocd. with **diabetes mellitus** in a mammal, which **method** comprises administering an effective non-toxic and pharmaceutically acceptable amt. of an insulin sensitizer and a sub-maximal amt. of an insulin secretagogue, to a mammal in need thereof; and a pharmaceutical compn. for use in such **method** are disclosed. The insulin secretagogue is esp. sulfonylurea. The insulin sensitizer is esp. 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione (I). Tablet formulations contg. I maleate are given.

IT 122320-73-4

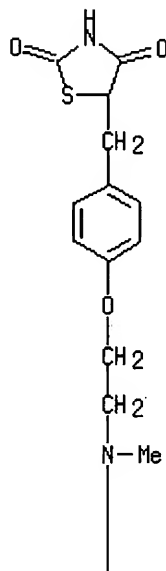
RL: THU (Therapeutic use); BSU (Biological study, unclassified);
 THU (Therapeutic use); BIOL (Biological study); PROC (Process);
 USES (Uses)

(as insulin sensitizer; treatment of **diabetes** with insulin sensitizer thiazolidinedione and insulin secretagogue sulfonylurea)

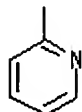
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT:

8

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 1999:9712 HCAPLUS
DOCUMENT NUMBER: 130:61091
TITLE: Treatment of **diabetes** with thiazolidinedione and sulfonylurea
INVENTOR(S): Smith, Stephen Alistair
PATENT ASSIGNEE(S): Smithkline Beecham Plc, UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 9857649</u>	<u>A1</u>	<u>19981223</u>	<u>WO 1998-EP3688</u>	<u>19980615</u>
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
<u>AU 9885392</u>	<u>A1</u>	<u>19990104</u>	<u>AU 1998-85392</u>	<u>19980615</u>
<u>EP 999845</u>	<u>A1</u>	<u>20000517</u>	<u>EP 1998-936363</u>	<u>19980615</u>
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
BR 9810142	A	20000808	BR 1998-10142	19980615
JP 2001523270	T2	20011120	JP 1999-503754	19980615
ZA 9805236	A	20000217	ZA 1998-5236	19980617
NO 9906264	A	20000217	NO 1999-6264	19991217
US 2001049380	A1	20011206	US 2001-848511	20010502
<u>PRIORITY APPLN. INFO.:</u>			GB 1997-12854	A 19970618
			GB 1998-6710	A 19980327
			WO 1998-EP3688	W 19980615
			US 1999-445859	B1 19991215

AB A **method** for the treatment of **diabetes mellitus** and conditions assocd. with **diabetes mellitus** in a mammal, which **method** comprises administering an effective nontoxic and pharmaceutically acceptable amt. of an insulin sensitizer and an insulin secretagogue, to a mammal in need thereof.

IT 155141-29-0, Rosiglitazone maleate

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(treatment of **diabetes** with thiazolidinedione and sulfonylurea)

RN 155141-29-0 HCAPLUS

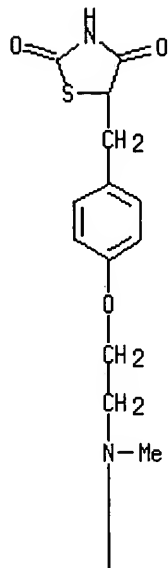
CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

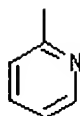
CRN 122320-73-4

CMF C18 H19 N3 O3 S

PAGE 1-A



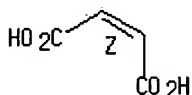
PAGE 2-A



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 1999:9699 HCAPLUS
DOCUMENT NUMBER: 130:61090
TITLE: Treatment of **diabetes** with rosiglitazone and insulin
INVENTOR(S): Smith, Stephen Alistair
PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9857636 **A1 19981223** **WO 1998-EP3692** **19980615**
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9882163 **A1 19990104** **AU 1998-82163** **19980615**
EP 999837 **A1 20000517** **EP 1998-932169** **19980615**
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, FI, RO
BR 9810444 A 20000905 BR 1998-10444 19980615
JP 2002504138 T2 20020205 JP 1999-503757 19980615
ZA 9805237 A 20000217 ZA 1998-5237 19980617
NO 9906265 A 19991217 NO 1999-6265 19991217
US 2002028768 A1 20020307 US 2001-928326 20010813

PRIORITY APPLN. INFO.:

GB 1997-12866 A 19970618
WO 1998-EP3692 W 19980615
US 1999-445858 B1 19991215

AB A **method** for the treatment of **diabetes mellitus** and conditions
assocd. with **diabetes mellitus** in a mammal, which **method** comprises
administering an effective nontoxic and pharmaceutically acceptable amt.
of insulin sensitizer rosiglitazone and insulin to a mammal in need
thereof.

IT **155141-29-0**, Rosiglitazone maleate

RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (**Therapeutic use**); BIOL (Biological
study); USES (Uses)

(treatment of **diabetes mellitus** with rosiglitazone
and insulin)

RN 155141-29-0 HCAPLUS

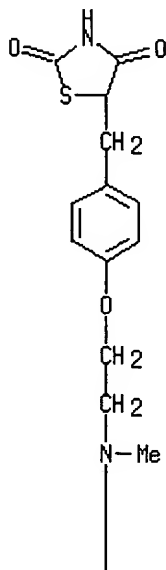
CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met
hyl]-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

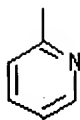
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CMF C18 H19 N3 O3 S

PAGE 1-A



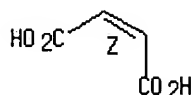
PAGE 2-A



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 17 HCAPLUS COPYRIGHT 2002 ACS

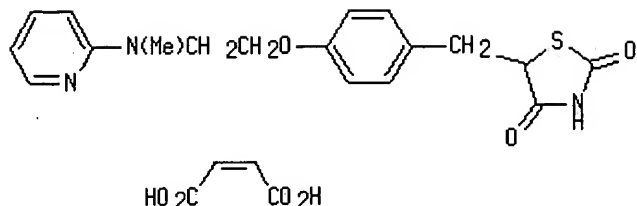
Full Text Citing References

ACCESSION NUMBER: 1999:9698 HCAPLUS
DOCUMENT NUMBER: 130:76189
TITLE: Treatment of **diabetes** with thiazolidinedione and alpha-glucosidase inhibitor
INVENTOR(S): Smith, Stephen Alistair
PATENT ASSIGNEE(S): Smithkline Beecham Plc, UK
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9857635	A1	19981223	WO 1998-EP3691	19980615
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9887999	A1	19990104	AU 1998-87999	19980615
EP 975343	A1	20000202	EP 1998-939513	19980615
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
BR 9810186	A	20000808	BR 1998-10186	19980615
JP 2001523271	T2	20011120	JP 1999-503756	19980615
ZA 9805235	A	20000217	ZA 1998-5235	19980617
NO 9906270	A	19991217	NO 1999-6270	19991217
US 2001034356	A1	20011025	US 2001-863136	20010523
US 2002123514	A1	20020905	US 2002-91008	20020305
PRIORITY APPLN. INFO.:			GB 1997-12865	A 19970618
			GB 1998-6708	A 19980327
			WO 1998-EP3691	W 19980615

US 1999-445951 B1 19991215
US 2001-863136 B1 20010523

GI



AB A **method** for the treatment of **diabetes mellitus** and conditions assocd. with **diabetes mellitus** in a mammal, which **method** comprises administering an effective non-toxic and pharmaceutically acceptable amt. of an insulin sensitizer (I) and an α -glucosidase inhibitor antihyperglycemic agent. The effects of α -glucosidase inhibitor acarbose on the pharmacokinetics of I in healthy humans are described along with pharmaceutical formulations (concns. and tablets) contg. I.

IT 155141-29-0

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(treatment of **diabetes mellitus** and conditions assocd. with **diabetes** with thiazolidinedione deriv. and α -glucosidase inhibitors)

RN 155141-29-0 HCAPLUS

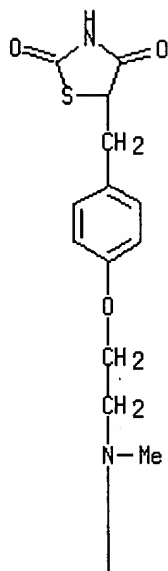
CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

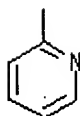
CRN 122320-73-4

CMF C18 H19 N3 O3 S

PAGE 1-A



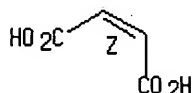
PAGE 2-A



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 17 HCAPLUS COPYRIGHT 2002 ACS

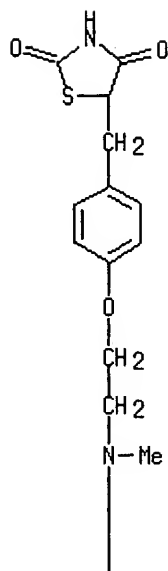
Full Text Citing References

ACCESSION NUMBER: 1999:9697 HCAPLUS
DOCUMENT NUMBER: 130:61089
TITLE: Treatment of **diabetes** with thiazolidinedione and metformin
INVENTOR(S): Smith, Stephen Alistair
PATENT ASSIGNEE(S): Smithkline Beecham Plc, UK
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

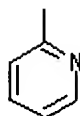
PATENT NO. KIND DATE APPLICATION NO. DATE

<u>WO 9857634</u>	<u>A1</u>	<u>19981223</u>	<u>WO 1998-EP3690</u>	<u>19980615</u>
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,				
DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,				
KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,				
NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,				
UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,				
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,				
CM, GA, GN, ML, MR, NE, SN, TD, TG				
<u>AU 9885393</u>	<u>A1</u>	<u>19990104</u>	<u>AU 1998-85393</u>	<u>19980615</u>
<u>EP 996444</u>	<u>A1</u>	<u>20000503</u>	<u>EP 1998-936364</u>	<u>19980615</u>
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				
IE, SI, FI, RO				
<u>BR 9810172</u>	<u>A</u>	<u>20000808</u>	<u>BR 1998-10172</u>	<u>19980615</u>
<u>JP 2002504137</u>	<u>T2</u>	<u>20020205</u>	<u>JP 1999-503755</u>	<u>19980615</u>
<u>ZA 9805238</u>	<u>A</u>	<u>20000217</u>	<u>ZA 1998-5238</u>	<u>19980617</u>
<u>NO 9906266</u>	<u>A</u>	<u>19991217</u>	<u>NO 1999-6266</u>	<u>19991217</u>
<u>US 2002004515</u>	<u>A1</u>	<u>20020110</u>	<u>US 2001-925394</u>	<u>20010809</u>
<u>US 2002137772</u>	<u>A1</u>	<u>20020926</u>	<u>US 2002-99161</u>	<u>20020313</u>
<u>PRIORITY APPLN. INFO.:</u>			<u>GB 1997-12857</u>	<u>A</u> <u>19970618</u>
			<u>GB 1998-6706</u>	<u>A</u> <u>19980327</u>
			<u>WO 1998-EP3690</u>	<u>W</u> <u>19980615</u>
			<u>US 1999-446030</u>	<u>B1</u> <u>19991215</u>
			<u>US 2001-925394</u>	<u>B1</u> <u>20010809</u>
AB	A method for the treatment and/or prophylaxis of diabetes mellitus , conditions assocd. with diabetes mellitus , and certain complications thereof, in a mammal which method comprises administering an effective nontoxic and pharmaceutically acceptable amt. of an insulin sensitizer rosiglitazone (I) and a biguanide antihyperglycemic agent such as metformin. Pharmacokinetics of I and metformin administered alone or in combination are described. Formulations for prepg. tablets contg. I is presented.			
IT	<u>155141-29-0</u> , Rosiglitazone maleate			
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)			
	(treatment of diabetes with thiazolidinedione insulin sensitizer and metformin)			
RN	<u>155141-29-0</u> HCAPLUS			
CN	2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)			
CM	1			
CRN	<u>122320-73-4</u>			
CMF	C18 H19 N3 O3 S			

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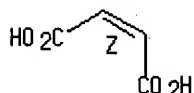
PAGE 2-A



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 1998:764284 HCAPLUS
DOCUMENT NUMBER: 130:10664
TITLE: Use of 5-(4-(2-(N-methyl-N-(2-pyridyl)amino)ethoxy)benzyl)-2,4-thiazolidinedione in the treatment of polycystic ovary syndrome and gestational **diabetes**
INVENTOR(S): Antonucci, Tammy; Lockwood, Dean; Norris, Rebecca
PATENT ASSIGNEE(S): Warner-Lambert Company, USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 9851305</u>	<u>A1</u>	<u>19981119</u>	<u>WO 1998-US10113</u>	<u>19980514</u>
W: AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
<u>ZA 9804084</u>	<u>A</u>	<u>19981120</u>	<u>ZA 1998-4084</u>	<u>19980514</u>
<u>AU 9874949</u>	<u>A1</u>	<u>19981208</u>	<u>AU 1998-74949</u>	<u>19980514</u>
<u>AU 731690</u>	B2	20010405		
<u>EP 981346</u>	A1	20000301	<u>EP 1998-922391</u>	19980514
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
<u>BR 9809120</u>	A	20000801	<u>BR 1998-9120</u>	19980514
<u>JP 2001525827</u>	T2	20011211	<u>JP 1998-549654</u>	19980514
<u>AU 9952576</u>	A1	19991202	<u>AU 1999-52576</u>	19991001
<u>AU 749416</u>	B2	20020627		
<u>NO 9905549</u>	A	19991112	<u>NO 1999-5549</u>	19991112
			<u>US 1997-856987</u>	A 19970515
			<u>AU 1997-17709</u>	A3 19970403
			<u>WO 1998-US10113</u>	W 19980514

PRIORITY APPLN. INFO.:

AB Novel **methods** of using thiazolidinone derivs. and related antihyperglycemic agents to treat populations at risk for developing noninsulin-dependent **diabetes mellitus** (NIDDM) and complications arising therefrom are disclosed. In one embodiment, the compds. of the invention are used to treat polycystic ovary syndrome to prevent or delay the onset of noninsulin-dependent **diabetes mellitus**. In another embodiment, the compds. of the invention are used to treat gestational **diabetes** to prevent or delay the onset of noninsulin-dependent **diabetes mellitus**.

IT 122320-73-4

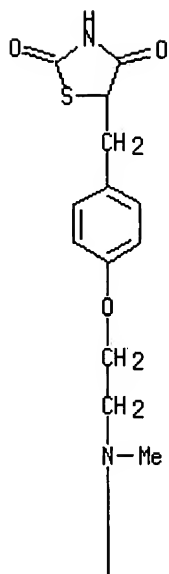
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (**Therapeutic use**); BIOL (Biological study); USES (Uses)

(ste ns treatment of polycystic ovary syndrome and gestational **diabetes** and prevention of NIDDM development by (methyl)pyridyl)

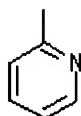
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 1998:672463 HCAPLUS
DOCUMENT NUMBER: 129:270626
TITLE: **Methods** and compositions for treating and/or preventing non-insulin dependent **diabetes mellitus** (NIDDM) using specific retinoid compounds
INVENTOR(S): Pfahl, Magnus; Lernhardt, Waldemar; Fanjol, Andrea
PATENT ASSIGNEE(S): Centre International de Recherches Dermatologiques Galderma, Fr.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 9842340</u>	<u>A1</u>	<u>19981001</u>	<u>WO 1998-US5591</u>	<u>19980324</u>
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
<u>AU 9865763</u>	<u>A1</u>	<u>19981020</u>	<u>AU 1998-65763</u>	<u>19980324</u>

EP 1019049	A1	20000719	EP 1998-911919	19980324
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9808054	A	20001107	BR 1998-8054	19980324
JP 2001521551	T2	20011106	JP 1998-545851	19980324
NO 9904612	A	19991124	NO 1999-4612	19990902

PRIORITY APPLN. INFO.:

US 1997-35604P	P	19970324
WO 1998-US5591	W	19980324

AB **Methods** are provided for treating and/or preventing non-insulin dependent **diabetes mellitus** (NIDDM) in subjects having or at substantial risk of developing NIDDM, using specific retinoid compds. that are structurally related to 9-cis retinoid acid which induce the differentiation of preadipocytes into adipocytes. These compds. may be administered alone or in combination with other anti-**diabetogenic** agents such as thiazolidinediones.

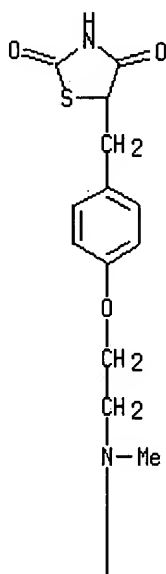
IT **122320-73-4**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (**Therapeutic use**); BIOL (Biological study); USES (Uses)
(retinoid compds. with other agents for treating and/or preventing non-insulin dependent **diabetes mellitus**)

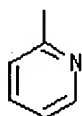
RN **122320-73-4** HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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L9 ANSWER 13 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 1998:41808 HCAPLUS
DOCUMENT NUMBER: 128:123811
TITLE: Use of thiazolidinedione derivatives and related

antihyperglycemic agents in the treatment of
insulin-resistant subjects with normal glucose
tolerance in order to prevent or delay the onset of
noninsulin-dependent **diabetes mellitus**

INVENTOR(S): Olefsky, Jerrold M.
PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan
SOURCE: U.S., 16 pp.
CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>US 5708012</u>	A	19980113	<u>US 1995-431266</u>	19950428

OTHER SOURCE(S): MARPAT 128:123811

AB **Methods** are disclosed for using thiazolidinone derivs. and related antihyperglycemic agents to treat populations exhibiting insulin-resistant non-impaired glucose tolerance in order to prevent or delay the onset of noninsulin-dependent **diabetes mellitus** and complications arising therefrom. In an outpatient trial with nondiabetic, obese patients, some of whom had impaired glucose tolerance, (+)-5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl)methyl]-2,4-thiazolidinedione (troglitazone) normalized glucose tolerance and markedly improved insulin resistance and hyperinsulinemia.

IT 122320-73-4

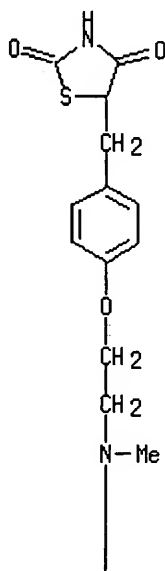
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(thiazolidinedione derivs. and related antihyperglycemic agents in treatment of insulin-resistant subjects with normal glucose tolerance to prevent or delay onset of noninsulin-dependent **diabetes mellitus**)

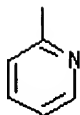
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl)methyl]- (9CI) (CA INDEX NAME)

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L9 ANSWER 14 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 1997:329275 HCAPLUS
 DOCUMENT NUMBER: 126:308792
 TITLE: Treating NIDDM with RXR agonists
 INVENTOR(S): Heyman, Richard A.; Cesario, Rosemary; Mukherjee, Ranjan
 PATENT ASSIGNEE(S): Ligand Pharmaceuticals Incorporated, USA
 SOURCE: PCT Int. Appl., 56 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 9710819</u>	<u>A1</u>	<u>19970327</u>	<u>WO 1996-US14904</u>	<u>19960917</u>
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
<u>CA 2232288</u>	<u>AA</u>	<u>19970327</u>	<u>CA 1996-2232288</u>	<u>19960917</u>
<u>AU 9670742</u>	<u>A1</u>	<u>19970409</u>	<u>AU 1996-70742</u>	<u>19960917</u>
AU 725998	B2	20001026		
<u>EP 859608</u>	<u>A1</u>	<u>19980826</u>	<u>EP 1996-931613</u>	<u>19960917</u>
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
<u>BR 9610624</u>	<u>A</u>	<u>19990316</u>	<u>BR 1996-10624</u>	<u>19960917</u>
<u>JP 11511472</u>	<u>T2</u>	<u>19991005</u>	<u>JP 1996-512842</u>	<u>19960917</u>
<u>US 6028052</u>	<u>A</u>	<u>20000222</u>	<u>US 1996-710309</u>	<u>19960917</u>
<u>US 5972881</u>	<u>A</u>	<u>19991026</u>	<u>US 1997-979725</u>	<u>19971126</u>
<u>NO 9801192</u>	<u>A</u>	<u>19980518</u>	<u>NO 1998-1192</u>	<u>19980317</u>
<u>US 6228862</u>	<u>B1</u>	<u>20010508</u>	<u>US 1999-309370</u>	<u>19990511</u>
<u>US 6316404</u>	<u>B1</u>	<u>20011113</u>	<u>US 2000-745681</u>	<u>20001222</u>

PRIORITY APPLN. INFO.:

US 1995-3869P	P	19950918
US 1995-4897P	P	19951006
US 1996-9884P	P	19960110
US 1996-18318P	P	19960524
US 1996-21839P	P	19960710
US 1996-710309	B3	19960917
WO 1996-US14904	W	19960917
US 1997-979725	A1	19971126
US 1999-309370	A3	19990511

AB This invention relates to **methods** and compns. for the treatment of non-insulin-dependent **diabetes mellitus** using an RXR agonist alone or in combination with a PPARy agonist such as thiazolidine dione compd. Example RXR agonists are LGD 1069, ALRT 1957 and LG 100268.

IT 122320-73-4, BRL 49653

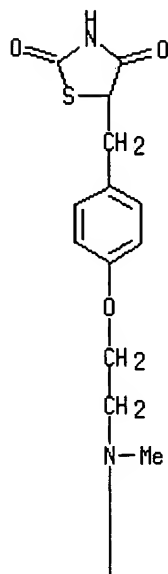
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
 (noninsulin dependent **diabetes** treatment with RXR agonists)

RN 122320-73-4 HCAPLUS

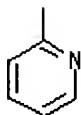
CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]met

hyl]- (9CI) (CA INDEX NAME)

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L9 ANSWER 15 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 1997:231131 HCAPLUS
 DOCUMENT NUMBER: 126:207528
 TITLE: A thiazolidione derivative for reducing the amount of exogenous insulin administered to a patient having noninsulin-dependent **diabetes mellitus**
 INVENTOR(S): Whitcomb, Randall W.
 PATENT ASSIGNEE(S): Warner-Lambert Company, USA; Whitcomb, Randall W.
 SOURCE: PCT Int. Appl., 43 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 9705875</u>	A2	19970220	<u>WO 1996-US12430</u>	19960729
<u>WO 9705875</u>	A3	19970327		
W: AU, BG, CA, CN, CZ, EE, GE, HU, IL, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, UZ, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
<u>CA 2221241</u>	AA	19970220	<u>CA 1996-2221241</u>	19960729
<u>AU 9666411</u>	A1	19970305	<u>AU 1996-66411</u>	19960729
<u>AU 724989</u>	B2	20001005		
<u>EP 851757</u>	A2	19980708	<u>EP 1996-926171</u>	19960729
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI				
<u>CN 1192683</u>	A	19980909	<u>CN 1996-196191</u>	19960729
<u>JP 11510508</u>	T2	19990914	<u>JP 1996-508479</u>	19960729
<u>NO 9800556</u>	A	19980209	<u>NO 1998-556</u>	19980209
PRIORITY APPLN. INFO.:			<u>US 1995-2098P</u>	P 19950810
			<u>WO 1996-US12430</u>	W 19960729

OTHER SOURCE(S): MARPAT 126:207528

AB This invention provides a **method** of reducing the amt. of exogenous insulin administered to a patient having noninsulin-dependent **diabetes mellitus** by administering to a patient a therapeutically effective amt. of a thiazolidione deriv. and/or a related compd. Seventeen patients with noninsulin-dependent **diabetes mellitus** that were still on insulin were treated with thiazolidinedione deriv. (400 mg/day) for 8 wk. Ten patients have had a mean decrease of 45% (39 units) in their daily dose of insulin and appear to be continuing to reduce their insulin requirements. At the same time, their glycemic control was improving with a mean decrease of 15% (36 mg/dL) in blood glucose. A total of 7 patients have had their insulin discontinued after 8 wk.

IT 122320-73-4, BRL 49653

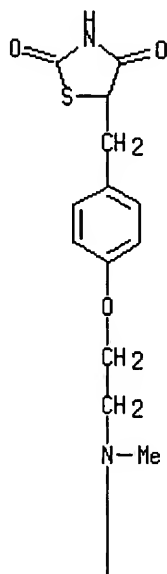
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(thiazolidione deriv. and/or related compds. for reducing amt. of exogenous insulin in humans with noninsulin-dependent **diabetes mellitus**)

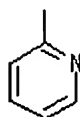
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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Full Text	Citing References
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ACCESSION NUMBER: 1996:713048 HCAPLUS
 DOCUMENT NUMBER: 125:319877
 TITLE: Adipocyte containing ob gene promoter for screening modulators useful in treatment of anorexia, obesity, and other diseases
 INVENTOR(S): Briggs, Michael R.; Auwerx, Johan; De Vos, Piet; Staels, Bart; Croston, Glenn E.; Miller, Stephen G.
 PATENT ASSIGNEE(S): Ligand Pharmaceuticals Incorporated, USA; Institut Pasteur De Lille
 SOURCE: PCT Int. Appl., 166 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 9629405</u>	<u>A2</u>	<u>19960926</u>	<u>WO 1996-US3808</u>	<u>19960319</u>
<u>WO 9629405</u>	<u>A3</u>	<u>19961128</u>		
W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML			
<u>CA 2215387</u>	<u>AA</u>	<u>19960926</u>	<u>CA 1996-2215387</u>	<u>19960319</u>
<u>AU 9655248</u>	<u>A1</u>	<u>19961008</u>	<u>AU 1996-55248</u>	<u>19960319</u>
<u>EP 815230</u>	<u>A2</u>	<u>19980107</u>	<u>EP 1996-912428</u>	<u>19960319</u>

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI

PRIORITY APPLN. INFO.:

<u>US 1995-408584</u>	A	19950320
<u>US 1995-418096</u>	A	19950405
<u>US 1995-510584</u>	A	19950802
<u>US 1995-558588</u>	A	19951030
<u>US 1995-7390P</u>	P	19951121
<u>US 1995-7721P</u>	P	19951130
<u>US 1995-8601P</u>	P	19951214
<u>WO 1996-US3808</u>	W	19960319

AB This invention relates to the isolation and cloning of the promoter and other control regions of a human ob gene. It provides a **method** for identifying and screening for agents useful for the treatment of diseases and pathol. conditions affected by the level of expression of an ob gene. These agents interact directly or indirectly with the promoter or other control regions of the ob gene. A PPARy agonist, BRL49653, has been identified to be useful in treating anorexia, cachexia, and other diseases characterized by insufficient food intake or body wt. loss. Modulators of ob gene expression may be used to treat other diseases such as obesity, **diabetes**, hypertension, cardiovascular diseases and infertility.

IT 122320-73-4, BRL49653

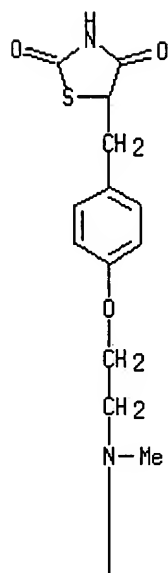
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(PPARy agonist; adipocyte contg. ob gene promoter for screening modulators useful in treatment of anorexia, obesity, and other diseases)

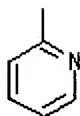
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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L9 ANSWER 17 OF 17 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

ACCESSION NUMBER: 1996:71475 HCAPLUS
 DOCUMENT NUMBER: 124:106679
 TITLE: Thiazolidinedione derivatives and related antihyperglycemic agents in the treatment of impaired glucose tolerance to prevent or delay the onset of noninsulin-dependent **diabetes mellitus**
 INVENTOR(S): Olefsky, Jerrold; Antonucci, Tammy; Lockwood, Dean; Norris, Rebecca
 PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan
 SOURCE: U.S., 15 pp. Cont.-in-part of U.S. Ser. No. 122,251, abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 7
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>US 5478852</u>	A	19951226	<u>US 1994-293899</u>	19940823
US 5478852	C1	20010313		
<u>WO 9507697</u>	A2	19950323	<u>WO 1994-US10187</u>	19940909
WO 9507697	A3	19950511		
W: AU, CA, CN, CZ, FI, HU, JP, KR, NO, NZ, RU, SK				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
<u>WO 9507694</u>	A1	19950323	<u>WO 1994-US10389</u>	19940914
W: AU, CA, CN, CZ, FI, HU, JP, KR, MW, NO, NZ, RU				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
<u>AU 9478351</u>	A1	19950403	<u>AU 1994-78351</u>	19940914

AU 679572	B2	19970703		
<u>EP 719140</u>	<u>A1</u>	<u>19960703</u>	<u>EP 1994-929204</u>	<u>19940914</u>
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
<u>CN 1134669</u>	<u>A</u>	<u>19961030</u>	<u>CN 1994-194058</u>	<u>19940914</u>
<u>JP 09502727</u>	<u>T2</u>	<u>19970318</u>	<u>JP 1995-509333</u>	<u>19940914</u>
<u>JP 3081245</u>	B2	20000828		
<u>HU 75874</u>	<u>A2</u>	<u>19970528</u>	<u>HU 1996-653</u>	<u>19940914</u>
<u>CZ 283207</u>	<u>B6</u>	<u>19980114</u>	<u>CZ 1996-2822</u>	<u>19940914</u>
<u>CZ 283208</u>	<u>B6</u>	<u>19980114</u>	<u>CZ 1996-2823</u>	<u>19940914</u>
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<u>JP 2000239167</u>	A2	20000905	<u>JP 2000-71978</u>	<u>19940914</u>
<u>JP 2000273043</u>	A2	20001003	<u>JP 2000-71977</u>	<u>19940914</u>
<u>NO 9601041</u>	<u>A</u>	<u>19960514</u>	<u>NO 1996-1041</u>	<u>19960314</u>
<u>FI 9601213</u>	<u>A</u>	<u>19960514</u>	<u>FI 1996-1213</u>	<u>19960315</u>
<u>AU 9717709</u>	<u>A1</u>	<u>19970529</u>	<u>AU 1997-17709</u>	<u>19970403</u>
<u>AU 706947</u>	B2	19990701		
<u>AU 9717710</u>	<u>A1</u>	<u>19970529</u>	<u>AU 1997-17710</u>	<u>19970403</u>
<u>AU 9952576</u>	A1	19991202	<u>AU 1999-52576</u>	<u>19991001</u>
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<u>NO 2000002963</u>	A	20000609	<u>NO 2000-2963</u>	<u>20000609</u>
<u>NO 2000002964</u>	A	20000609	<u>NO 2000-2964</u>	<u>20000609</u>

PRIORITY APPLN. INFO.:

<u>US 1993-122251</u>	B2	19930915
<u>US 1994-292585</u>	A	19940823
<u>US 1994-293899</u>		19940823
<u>JP 1994-509333</u>	A3	19940914
<u>JP 1995-509333</u>	A3	19940914
<u>WO 1994-US10389</u>	W	19940914
<u>AU 1997-17709</u>	A3	19970403

OTHER SOURCE(S): MARPAT 124:106679

AB Novel **methods** of using thiazolidinone derivs. and related antihyperglycemic agents to treat populations experiencing impaired glucose tolerance in order to prevent or delay the onset of noninsulin-dependent **diabetes mellitus** and complications arising therefrom, are disclosed. Effects of (+)-5-[[4-[(3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl)methoxy]phenyl]methyl]-2,4-thiazolidinedione (troglitazone) was clin. tested with patients with impaired glucose tolerance by the WHO criteria; the results showed that treatment with troglitazone correlated to redn. of fasting insulin levels and return of glucose tolerance to the normal range for ~70% of the subjects.

IT 122320-73-4

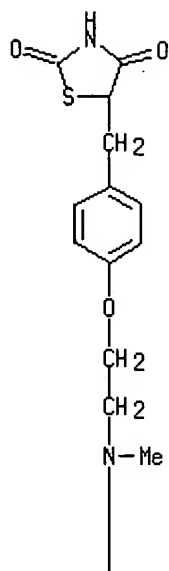
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(thiazolidinedione derivs. in prevention of onset of noninsulin-dependent **diabetes**)

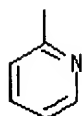
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



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FILE 'REGISTRY' ENTERED AT 20:08:18 ON 03 OCT 2002

L1 STRUCTURE UPLOADED

L2 2 S L1

L3 48 S L1 FULL

FILE 'HCAPLUS' ENTERED AT 20:14:30 ON 03 OCT 2002

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L7 56 S L6 AND DIAB?

L8 44 S L7 AND MELLIT?

L9 17 S L8 AND PD < MAY 20 1999

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490 L3

127960 POLYMO?

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11 BLACKLER, P?/AU

L11 3 L10 AND BLACKLER, P?/AU

=> d l11, ibib abs fhitrstr, 1-3

L11 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS

Full
Text

Citing
References

ACCESSION NUMBER: 2000:772629 HCAPLUS
 DOCUMENT NUMBER: 133:340315
 TITLE: Therapeutic action and properties of a **polymorphic** form of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, maleic acid salt
 INVENTOR(S): **Blackler, Paul David James**; Browne, Christine Marie; Coakley, Timothy G.; Giles, Robert Gordon; Morrissey, Gillian
 PATENT ASSIGNEE(S): SmithKline Beecham PLC, UK; SmithKline Beecham (Cork) Limited
 SOURCE: PCT Int. Appl., 21 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064896	A1	20001102	WO 2000-GB1520	20000419
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1173435	A1	20020123	EP 2000-920892	20000419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000009932	A	20020409	BR 2000-9932	20000419
NO 2001005147	A	20011217	NO 2001-5147	20011022
GB 1999-9473 A 19990423 GB 1999-12196 A 19990525 WO 2000-GB1520 W 20000419				

PRIORITY APPLN. INFO.:

AB A **polymorphic** form of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, maleic acid salt (the "**Polymorph**") characterized in that it provides: (i) an IR spectrum contg. peaks at 1763, 912, 856 and 709 cm⁻¹; and/or (ii) a Raman spectrum contg. peaks at 1762, 1284, 912 and 888 cm⁻¹; and/or (iii) a solid-state ¹³C NMR spectrum contg. peaks at 111.0, 113.6, 119.8, 129.1, 130.9, 131.8, 134.7, 138.7, 146.5, 152.7, 157.5, 169.5, 171.0, 178.7 ppm; and/or (iv) an x-ray powder diffraction (XRPD) pattern which gives calcd. lattice spacings at 5.87, 5.30, 4.69, 4.09, 3.88, 3.61, 3.53 and 3.46 Angstroms; a process for prepg. such a compd., a pharmaceutical compn. contg. such a compd. and the use of such a compd. in medicine.

IT 155141-29-0

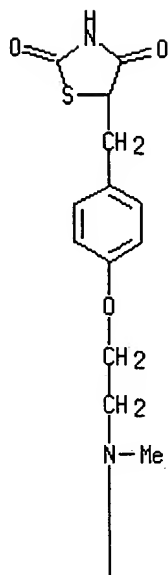
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antidiabetic action and properties of **polymorphic** form of [[(N-methyl-N-(pyridyl)amino)ethoxy]benzyl]thiazolidinedione maleate)
 RN 155141-29-0 HCAPLUS
 CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

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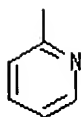
CRN 122320-73-4

CMF C18 H19 N3 O3 S

PAGE 1-A



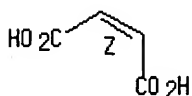
PAGE 2-A



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER:	2000:772627 HCAPLUS
DOCUMENT NUMBER:	133:340314
TITLE:	Therapeutic action and properties of a polymorphic form of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, maleic acid salt
INVENTOR(S):	Blackler, Paul David James ; Giles, Robert Gordon; Moore, Stephen; Sasse, Michael John
PATENT ASSIGNEE(S):	SmithKline Beecham PLC, UK
SOURCE:	PCT Int. Appl., 19 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064893	A2	20001102	WO 2000-GB1522	20000419
WO 2000064893	A3	20010125		
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1175418	A2	20020130	EP 2000-922793	20000419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000009935	A	20020416	BR 2000-9935	20000419
NO 2001005148	A	20011217	NO 2001-5148	20011022
<u>PRIORITY APPLN. INFO.:</u>				
			GB 1999-9471	A 19990423
			GB 1999-12195	A 19990525
			WO 2000-GB1522	W 20000419

AB A **polymorphic** form of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, maleic acid salt (the "**Polymorph**") characterized in that it provides: (i) an infra red spectrum contg. peaks at 1752, 1546, 1154, 621, and 602 cm⁻¹; and/or (ii) a Raman spectrum contg. peaks at 1751, 1243 and 602 cm⁻¹; and/or (iii) a solid-state NMR spectrum contg. peaks at 111.9, 114.8, 119.6, 129.2, 134.0, 138.0, 144.7, 153.2, 157.1, 170.7, 172.0 and 175.0 ppm; and/or (iv) an x-ray powder diffraction (XRPD) pattern which gives calcd. lattice spacings of 6.46, 5.39, 4.83, 4.68, 3.71, 3.63, 3.58, and 3.48 Angstroms; a process for prepg. such a compd., a pharmaceutical compn. contg. such a compd. and the use of such a compd. in medicine.

IT 168553-12-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antidiabetic action of **polymorphic** form of

[[(N-methyl-N-(pyridyl)amino)ethoxy]benzyl]thiazolidinedione maleate)

RN 168553-12-6 HCAPLUS

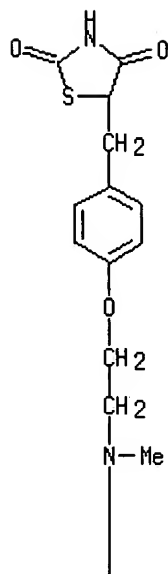
CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)

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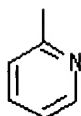
CRN 122320-73-4

CMF C18 H19 N3 O3 S

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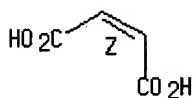
PAGE 2-A



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



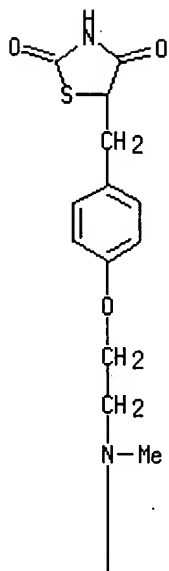
L11 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS

Full Text Citing References

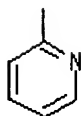
ACCESSION NUMBER: 2000:772626 HCAPLUS
DOCUMENT NUMBER: 133:340313
TITLE: Therapeutic action and properties of a **polymorphic** form of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, maleic acid salt
INVENTOR(S): **Blackler, Paul David James**; Giles, Robert Gordon; Sasse, Michael John
PATENT ASSIGNEE(S): SmithKline Beecham P.L.C., UK
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000064892	A2	20001102	WO 2000-GB1514	20000419
WO 2000064892	A3	20010125		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1173434	A2	20020123	EP 2000-920889	20000419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000009934	A	20020604	BR 2000-9934	20000419
NO 2001005149	A	20011217	NO 2001-5149	20011022
PRIORITY APPLN. INFO.:				
			GB 1999-9472	A 19990423
			GB 1999-12197	A 19990525
			WO 2000-GB1514	W 20000419
AB	A polymorphic form of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione, maleic acid salt (the " Polymorph ") characterized in that it: (i) provides an IR spectrum contg. peaks at 1360, 1326, 1241, 714 and 669 cm ⁻¹ ; and/or (ii) provides a Raman spectrum contg. peaks at 1581, 768, 670, 271 and 226 cm ⁻¹ ; and/or (iii) provides a solid-state NMR spectrum contg. peaks at chem. shifts substantially; and/or (iv) provides an x-ray powder diffraction (XRPD) pattern contg. peaks; a process for prepg. such a compd., a pharmaceutical compn. contg. such a compd. and the use of such a compd. in medicine.			
IT	168553-12-6			
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)			
	(antidiabetic action of polymorphic form of			
	[[(N-methyl-N-(pyridyl)amino)ethoxy]benzyl]thiazolidinedione maleate)			
RN	168553-12-6 HCAPLUS			
CN	2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, (2Z)-2-butenedioate (9CI) (CA INDEX NAME)			
CM	1			
CRN	122320-73-4			
CMF	C18 H19 N3 O3 S			

PAGE 1-A



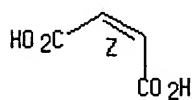
PAGE 2-A



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



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L1 STRUCTURE UPLOADED

L2 2 S L1

L3 48 S L1 FULL

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L4 490 S L3

L5 324 S L3/THU

L6 92 S L5 AND METHOD

L7 56 S L6 AND DIAB?

L8 44 S L7 AND MELLIT?

L9 17 S L8 AND PD < MAY 20 1999

L10 7 S L3 AND POLYMO?

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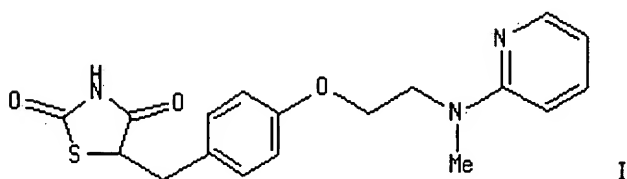
L12 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2002 ACS

Full Citing
Text References

ACCESSION NUMBER: 2002:504785 HCAPLUS
DOCUMENT NUMBER: 137:83621
TITLE: Preparation and use of 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione methanesulfonate
INVENTOR(S): Craig, Andrew Simon; Ho, Tim Chien Ting; Millan, Michael; O'Keeffe, Deirdre
PATENT ASSIGNEE(S): Smithkline Beecham P.L.C., UK
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002051839	A1	20020704	WO 2001-GB5751	20011221
<p>W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM</p> <p>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG</p>				
PRIORITY APPLN. INFO.:			GB 2000-31521	A 20001222
			GB 2000-31524	A 20001222
			GB 2000-31526	A 20001222
			GB 2000-31528	A 20001222

GI



AB A compd. 5-[4-[2-(N-methyl-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione (I) methanesulfonate salt (II) or solvate thereof; a process for prepg. I, a compn. comprising I and its therapeutic use is disclosed. Four **polymorphic** forms were prepd. and characterized. For instance, MsOH (0.54 mL) was added to a mixt. of I (3.0 g) in EtOAc (60 mL) and was heated with agitation to reflux to give a suspension. The resulting mixt. was cooled to 21°C, the solid formed collected by filtration, washed with EtOAc and dried under vacuum for 16 h (3.73 g yield). **Polymorphic** forms I-IV were characterized by at least one of the following means: aq. soly., m.p., 1H-NMR (soln.), 13C-NMR (solid state), IR/Raman spectra, XRPD and DSC. II is a stable solid with good water soly., desirable flow properties and is amenable to large scale processing (milling). II is useful for the prevention/treatment of diabetes mellitus.

IT **439902-56-4P**

RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(polymorphic forms I-IV characterized; prepn. and characterization of 5-[4-[2-(N-Me-N-(2-pyridyl)amino)ethoxy]benzyl]thiazolidine-2,4-dione methanesulfonate)

RN 439902-56-4 HCAPLUS

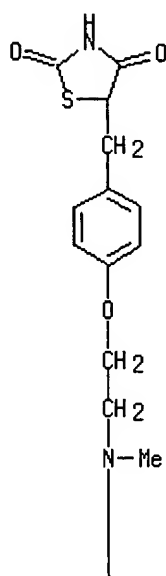
CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

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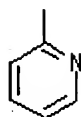
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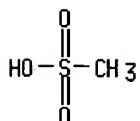
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CRN 75-75-2

CMF C H4 O3 S



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

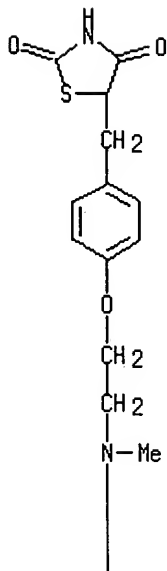
L12 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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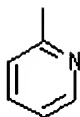
ACCESSION NUMBER: 2002:256258 HCAPLUS
DOCUMENT NUMBER: 136:299688
TITLE: Novel **polymorphic** forms of 5-[4-[2-[N-methyl-N-(2-pyridyl)amino]ethoxy]benzyl] thiazolidine-2,4-dione maleate and process for their preparation
INVENTOR(S): Chebiyyam, Prabhakar; Mamillapalli, Ramabhadra Sarma; Krishnamurthi, Vyas; Seella, Vishnuvardhan Reddy; Gaddam, Om Reddy
PATENT ASSIGNEE(S): Reddy's Research Foundation, India; Cord, Janet I.
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002026737	A1	20020404	WO 2001-US29896	20010925
<p>W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM</p> <p>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG</p>				
AU 2001091232	A5	20020408	AU 2001-91232	20010925
<p>PRIORITY APPLN. INFO.: IN 2000-MA805 A 20000926 WO 2001-US29896 W 20010925</p>				
<p>AB This invention relates to novel polymorphic/pseudopolymorphic forms of 5-[4-[2-[N-methyl-N-(2-pyridyl)amino]ethoxy]benzyl] thiazolidine-2,4-dione maleate (I). The invention also relates to a pharmaceutical compn. comprising the novel polymorphic form or their mixt. and a pharmaceutically acceptable carrier. The polymorphic forms of the present invention are more active, as antidiabetic agent, than the hitherto known 5-[4-[2-[N-2-methyl-N-(2-pyridyl)amino]ethoxy]benzyl] thiazolidine-2,4-dione maleate. I was dissolved in ethanol and was allowed to cool to room temp. over a period of 18 h to yield 80% of >99% pure polymorphic form of I.</p>				
<p>IT 155141-29-0P RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (novel polymorphic forms of triazolidinedione maleate and process for their prepn.)</p>				
RN	155141-29-0 HCAPLUS			
CN	2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]-, (2Z)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)			
CM	1			
CRN	122320-73-4			
CMF	C18 H19 N3 O3 S			

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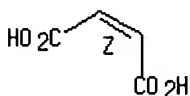
PAGE 2-A



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
ACCESSION NUMBER:	2001:724803 HCAPLUS
DOCUMENT NUMBER:	136:79548
TITLE:	Inhibition of RXR and PPAR γ ameliorates diet-induced obesity and type 2 diabetes
AUTHOR(S):	Yamauchi, Toshimasa; Waki, Hironori; Kamon, Junji; Murakami, Koji; Motojima, Kiyoto; Komeda, Kajuro; Miki, Hiroshi; Kubota, Naoto; Terauchi, Yasuo; Tsuchida, Atsuko; Tsuboyama-Kasaoka, Nobuyo; Yamauchi, Naoko; Ide, Tomohiro; Hori, Wataru; Kato, Shigeaki; Fukayama, Masashi; Akanuma, Yasuo; Ezaki, Osamu; Itai, Akiko; Nagai, Ryozi; Kimura, Satoshi; Tobe, Kazuyuki; Kagechika, Hiroyuki; Shudo, Koichi; Kadowaki, Takashi
CORPORATE SOURCE:	Department of Internal Medicine, Graduate School of Medicine, University of Tokyo, Tokyo, 113-8655, Japan

SOURCE: Journal of Clinical Investigation (2001), 108(7),
1001-1013
CODEN: JCINAO; ISSN: 0021-9738
PUBLISHER: American Society for Clinical Investigation
DOCUMENT TYPE: Journal
LANGUAGE: English

AB PPAR γ is a ligand-activated transcription factor and functions as a heterodimer with a retinoid X receptor (RXR). Supraphysiol. activation of PPAR γ by thiazolidinediones can reduce insulin resistance and hyperglycemia in type 2 diabetes, but these drugs can also cause wt. gain. Quite unexpectedly, a moderate redn. of PPAR γ activity obsd. in heterozygous PPAR γ -deficient mice or the Prol2Ala **polymorphism** in human PPAR γ , has been shown to prevent insulin resistance and obesity induced by a high-fat diet. In this study, we investigated whether functional antagonism toward PPAR γ /RXR could be used to treat obesity and type 2 diabetes. We show herein that an RXR antagonist and a PPAR γ antagonist decrease triglyceride (TG) content in white adipose tissue, skeletal muscle, and liver. These inhibitors potentiated leptin's effects and increased fatty acid combustion and energy dissipation, thereby ameliorating HF diet-induced obesity and insulin resistance. Paradoxically, treatment of heterozygous PPAR γ -deficient mice with an RXR antagonist or a PPAR γ antagonist depletes white adipose tissue and markedly decreases leptin levels and energy dissipation, which increases TG content in skeletal muscle and the liver, thereby leading to the re-emergence of insulin resistance. Our data suggested that appropriate functional antagonism of PPAR γ /RXR may be a logical approach to protection against obesity and related diseases such as type 2 diabetes.

IT 122320-73-4, Rosiglitazone

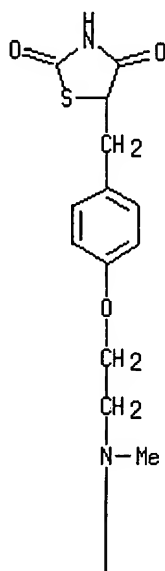
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibition of RXR and PPAR γ ameliorates diet-induced obesity and type 2 diabetes)

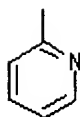
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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PAGE 2-A



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2002 ACS

Full Text	Citing References
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ACCESSION NUMBER: 1999:437778 HCAPLUS
 DOCUMENT NUMBER: 131:197757
 TITLE: Loss-of-function mutations in PPAR γ associated with human colon cancer
 AUTHOR(S): Sarraf, Pasha; Mueller, Elisabetta; Smith, Wendy M.; Wright, Harold M.; Kum, Jennifer B.; Aaltonen, Lauri A.; De la Chapelle, Albert; Spiegelman, Bruce M.; Eng, Charis
 CORPORATE SOURCE: Department of Cancer Biology Dana-Farber Cancer Institute Department of Cell Biology, Harvard Medical School, Boston, MA, 02115, USA
 SOURCE: Molecular Cell (1999), 3(6), 799-804
 CODEN: MOCEFL; ISSN: 1097-2765
 PUBLISHER: Cell Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The gamma isoform of the peroxisome proliferator-activated receptor, PPAR γ , regulates adipocyte differentiation and has recently been shown to be expressed in neoplasia of the colon and other tissues. The authors have found four somatic PPAR γ mutations among 55 sporadic colon cancers: one nonsense, one frameshift, and two missense mutations. Each greatly impaired the function of the protein. C.472delA results in deletion of the entire ligand binding domain. Q286P and K319X retain a total or partial ligand binding domain but lose the ability to activate transcription through a failure to bind to ligands. R288H showed a normal response to synthetic ligands but greatly decreased transcription and binding when exposed to natural ligands. These data indicate that colon cancer in humans is assocd. with loss-of-function mutations in PPAR γ .

IT 122320-73-4, BRL 49653

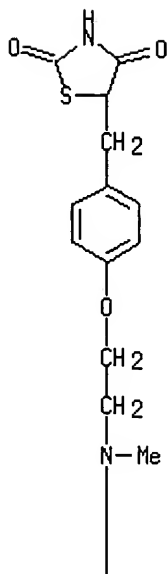
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(loss-of-function mutated PPAR γ assocd. with human colon cancer binding of and transactivation response to)

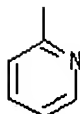
RN 122320-73-4 HCAPLUS

CN 2,4-Thiazolidinedione, 5-[[4-[2-(methyl-2-pyridinylamino)ethoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)

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FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
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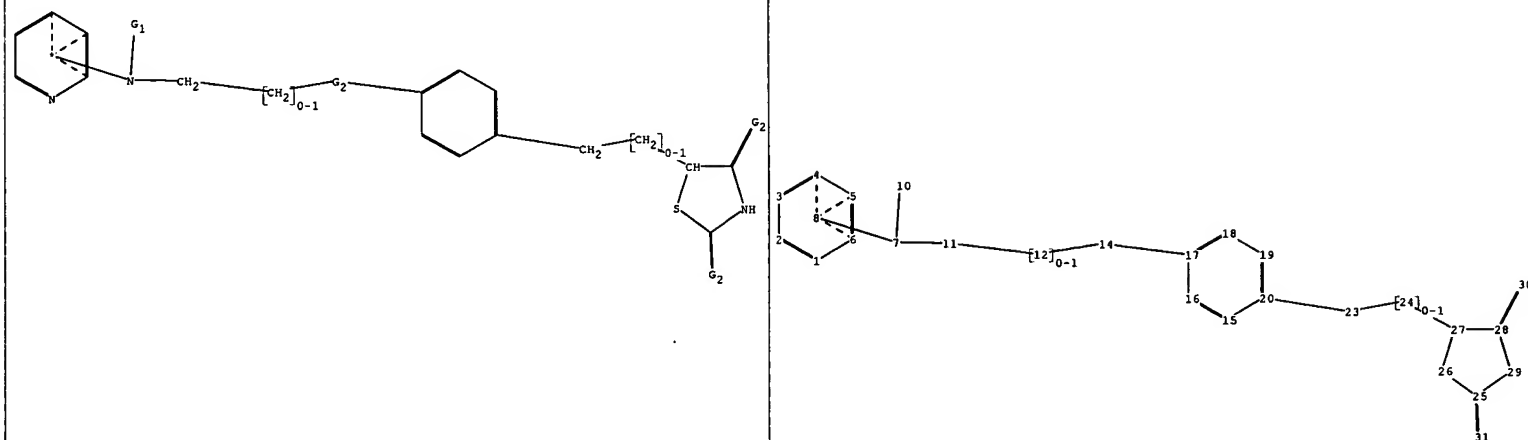
L4 490 S L3
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L6 92 S L5 AND METHOD
L7 56 S L6 AND DIAB? ;
L8 44 S L7 AND MELLIT?
L9 17 S L8 AND PD < MAY 20 1999
L10 7 S L3 AND POLYMO?
L11 3 S L10 AND BLACKLER, P?/AU
L12 4 S L10 NOT L11

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L13 0 L3

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chain nodes :

7 10 11 12 14 23 24 30 31

ring nodes :

1 2 3 4 5 6 15 16 17 18 19 20 25 26 27 28 29

chain bonds :

7-10 7-11 11-12 12-14 14-17 20-23 23-24 24-27 25-31 28-30

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20 25-26 25-29
26-27 27-28 28-29

exact/norm bonds :

7-10 12-14 14-17 25-29 25-31 28-29 28-30

exact bonds :

7-11 11-12 20-23 23-24 24-27 25-26 26-27 27-28

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20

isolated ring systems :

containing 1 : 15 : 25 :

G1:CH3,Et

G2:O,S

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 10:CLASS 11:CLASS
12:CLASS 14:CLASS 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:Atom 23:CLASS
24:CLASS 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:CLASS 31:CLASS